REMARKS

Entry of the foregoing and reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

As correctly reflected in the Office Action Summary, claims 1-6 are pending. After entry of the instant amendments, claims 1-6 and new claims 7-8 will be pending.

Claims 1 and 4-6 have been amended to clarify the subject matter which Applicants considers to be the claimed invention. This amendment is supported by the specification as originally filed; as well as at page 1, lines 6-16, page 3, lines 14-23, and the Example on pages 4-5 (disclosing that the present invention comprises the determination of the quantity of each species or type of virus within the claimed composition, and that the quantity is determined using a specific monoclonal antibody which binds to the composition).

New claims 7 and 8 are added herein. These new claims are supported in the specification at least at page 2, lines 34-39 and page 4, lines 1-5 (disclosing that the viruses present in the composition are propagated using serial dilutions of the composition); page 2, lines 3-5, page 3, lines 28-31 (disclosing that the present invention provides a method of titration where each virus species or virus types present in the composition is titrated without impacting quantity of the other virus species or types present in the composition); page 2, lines 6-15 and 34-39 (disclosing the step of propagating the viruses of the composition by adding the viruses to cell cultures in serial dilutions of the composition and culturing the cells); page 3, lines 14-27 (disclosing the step of determining, for each dilution, the amount of virus type or virus species present using a virus species or virus

type specific monoclonal antibody); and page 3, lines 24-27 (disclosing the step of performing the first two steps in parallel with monoclonal antibodies for each virus species or type).

Further, Applicants have amended the claims and crafted the new claims to recite virus "type", rather than "serotype". In support of the recitation of "type", Applicants respectfully submit page 114 from *Field's Virology*, 3d Ed., Philadelphia: Lippincott Williams & Wilkins (1996), which discusses that "serotype" and "type" may be used interchangeably. As *Field's Virology* is an very well known and respected reference in the virology art, Applicants submit that the fact that "type" and "serotype" are synonymous is readily known to the skilled artisan.

Accordingly, no prohibited new matter is believed to have been added by entry of the above amendments. The amendments to the claims have been made without prejudice to or disclaimer of the subject matter contained in the amended claims. Applicants reserve the right to file a divisional or continuation application on the material canceled by way of amendment.

Rejections under 35 U.S.C. § 112, Second Paragraph

Claim 6 stands rejected under 35 U.S.C. § 112, second paragraph, as purportedly indefinite. Specifically, the Office Action states that claim 6 lack antecedent basis because "types", rather than "serotypes", should be recited at line 2. Claim 6 has been amended to recite virus "types". Applicants respectfully submit that the rejection to claim 6 has been obviated.

Rejections under 35 U.S.C. 102(b)

Claims 1-4 stand rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Ibanez-Bernal *et al.* Claims 1-3 and 6 stand rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Shaw *et al.* Claim 5 stands rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Osterhaus *et al.* Applicants respectfully traverse the rejection to claims 1-6 and on behalf of new claims 7-8.

"[A]nticipation requires the presence in a single prior art disclosure of all elements of a claimed invention as arranged in the claims." *Jamesbury Corp. v. Litton Industrial Products, Inc.* 225 U.S.P.Q. 253, 256 (Fed. Cir. 1985). The cited references do not describe or suggest all of the elements of the rejected claims, as discussed in greater detail below.

The claimed invention

Before turning to the cited references, Applicants provide a discussion of the presently claimed invention.

The present invention addresses the problem of titration of a specific type or species of virus within a composition, such as a vaccine, which contains different species or types of one virus. For example, such a composition may contain different species or types of dengue virus, Rotavirus, or of polio virus. The present invention provides an efficient method of titrating the quantity of each virus type or species in the composition, such that the quantity of viruses of the other species which are also present are not affected (*see* new claim 8). The ability to titrate one virus type or species without affecting the other types or

species present in the same composition is novel and has not been accomplished prior to this invention. As discussed in the present specification on pages 1-2, this ability allows for quicker and less costly analysis of viral compositions and allows the manufacturer to exercise a high level of control over the quantities of virus in the product. This is especially important in the vaccine industry, where types and species of virus must be present in perfectly defined proportions.

As discussed on page 2 of the specification, the methods of the present invention are especially useful when the different types and species of virus in the composition are closely related antigenically. In such a case, neutralization of one type would often result in the neutralization of the other closely related types via cross-reaction. However, in the case of the presently claimed invention, the virus types and species are propagated on cells in serial dilutions of the composition of interest. Thus, the amounts of each type and species increase proportionally as the viruses are propagated. Then, the quantification is performed in parallel with monoclonal antibodies for each virus species or type. Thus, any cross reactivity will be limited such that the result is not adversely affected.

As amended herein, the present claims are directed to methods of determining quantity of a virus type or species in a composition which contains different species or types of live virus. The methods comprise propagating the viruses of each type or species on cells which are permissive for the viruses and which do not induce any viral interference. Next, the quantity of each virus species or type in the composition is determined using a specific monoclonal antibody, and the quantity of each type or species of virus of the composition bound by the specific antibody is determined. Each monoclonal

antibody is virus type or virus species specific. The propagation may be performed in serial dilutions of the composition.

The propagation step and the determination of amount of virus type or species may be performed in parallel with monoclonal antibodies for each virus species or type. Importantly, each virus species or virus types present in the composition is titrated without impacting quantity of the other virus species or types present in the composition.

Applicants submit that the cited references do not anticipate the claimed invention as described.

The cited references

Ibanez-Bernal *et al.*

Claims 1-4 stand rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Ibanez-Bernal *et al.* Specifically, Ibanez-Bernal *et al.* purportedly disclose that Vero cell cultured dengue virus serotypes 2 and 3 were identified by serotype-specific monoclonal antibodies and confirmed by RT-PCR. Applicants respectfully traverse the rejection to claims 1-4 and on behalf of new claims 7-8.

Applicants submit that the cited reference fails to recite all of the elements of claims 1-4, 7 and 8, and thus does not anticipate the claimed invention.

First, the claimed invention is directed to methods of determining virus quantity within a composition. This point is emphasized in the present amendment to claim 1, reciting "determining the quantity of each type or species of virus of the composition" in step (b) of independent claim 1, and "determining for each dilution the amount of virus type

or virus species" in step (b) in new independent claim 8. However, the cited reference fails to disclose or even suggest the determination of virus quantity within a composition, let alone the determination of quantity of specific virus species and types within a composition. In fact, the monoclonal antibodies of Ibanez-Bernal *et al.* are used for a qualitative determination of the viruses which are present, not for a quantitative determination. Specifically, Ibanez-Bernal *et al.* seek to determine the serotype of dengue virus found in mosquitos from city dumps and cemeteries. The cited reference is focused on the mosquitoes transmitting the dengue virus, from a qualitative, epidemiological perspective. The reference fails to disclose the quantification of different types of species of dengue virus found in the mosquitoes.

Although rejected claim 4, dependent upon claim 1, recites the titration of dengue virus, claim 4 contains all of the elements of claim 1. Thus, it is not anticipated by the cited reference.

With regard to new claims 7 and 8, the cited reference fails to disclose the claimed elements of performing the quantification using serial dilutions of the composition. Nor does the cited reference disclose the performance of the propagation of the viral composition and the quantification, in parallel with monoclonal antibodies for each specific virus species or type. Finally, the cited reference certainly fails to recite that each virus species or virus type present in the composition is titrated without impacting quantity of the other virus species or types present. Thus, the cited reference also fails to anticipate new claims 7-8.

Thus, as the cited reference fails to recite all of the elements of the claimed invention, Applicants respectfully request that the rejection be withdrawn.

Shaw *et al.*

Claims 1-3 and 6 stand rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Shaw *et al.* Specifically, Shaw *et al.* purportedly disclose serotype-specific monoclonal antibodies directed at VP7 in a competitive solid-phase immunoassay, to measure epitope specific responses to serotypes 1, 2 and 3 in the sera of children who received a serotype-3 Rotavirus vaccine. Applicants respectfully traverse the rejection to claims 1-3, 6 and on behalf of new claims 7-8.

Applicants note that the claimed invention, as recited in rejected claims 1-3 and 6, as well as new claims 7-8, is directed to the quantification of specific virus species and types within a single composition, using virus species or type specific monoclonal antibodies. The cited reference fails to disclose these elements.

Specifically, Shaw *et al.* is concerned with the potential of monoclonal antibodies that are specific of a certain protein, VP7. However, the VP7 protein is not specific to a specific virus type or species. On the contrary, as disclosed in the introduction on the left column of page 1 of Shaw *et al.*, the protein VP7 can be found on all three serotypes of Rotavirus at interest in the reference, serotypes 1, 2 and 3.

In addition, Shaw *et al.* fails to disclose the claimed element of quantification. Shaw *et al.* does not disclose the determination of the quantity of types or species of viruses in a composition. Rather, Shaw *et al.* discloses the determination of the antibodies which

are present in a serum. Further, Shaw *et al.* do not recite a method step of propagating the viruses on cells which do not produce interference.

With regard to new claims 7 and 8, the cited reference again fails to disclose the claimed elements of performing the quantification using serial dilutions of the composition. The cited reference also fails to disclose the performance of the propagation of the viral composition and the quantification, in parallel with monoclonal antibodies for each specific virus species or type. Finally, the cited reference certainly fails to recite that each virus species or virus types present in the composition is titrated without impacting quantity of the other virus species or types present in the composition. Thus, the cited reference also fails to anticipate new claims 7-8.

Thus, the cited reference fails to recite all of the elements of the claimed invention, and Applicants respectfully request that the rejection be withdrawn.

Osterhaus *et al.*

Claim 5 stands rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Osterhaus *et al.* Specifically, Osterhaus *et al.* purportedly disclose Lymphocyte hybridomas secreting monoclonal antibodies against different strains of polio virus (type 1, 2 and 3). Applicants respectfully traverse the rejection to claim 5 and on behalf of new claims 7-8.

Applicants note that the claimed invention, as recited in rejected claim 5, is directed to the quantification of specific polio virus species and types within a single composition,

using virus species or type specific monoclonal antibodies. The cited reference fails to disclose these elements.

Osterhaus *et al.* disclose the production of monoclonal antibodies against polio viruses. But, there is no disclosure or even a suggestion of the claimed method. The Office Action suggests that the disclosed monoclonal antibodies could be used in vaccine control, via the neutralization of the vaccine virus. Applicants respectfully note that this vaccine control test is disclosed on page 1 of the specification as what is known in the art, in contrast to what is the presently claimed invention.

Specifically, Osterhaus *et al.* fail to disclose the elements of a propagation step on cells. Osterhaus *et al.* further fail to disclose the claimed step directed to the quantitative determination of each type and species of polio virus present in the composition of interest.

Finally, with regard to new claims 7 and 8, the cited reference again fails to disclose the claimed elements of performing the quantification using serial dilutions, as well as the performance of the propagation of the viral composition and the quantification, in parallel with monoclonal antibodies for each specific virus species or type. Finally, the cited reference fails to recite that each virus species or virus types present in the composition is titrated without impacting the quantity of the other virus species or types present in the composition. Thus, the cited reference also fails to anticipate new claims 7-8.

Thus, the cited reference fails to recite all of the elements of the claimed invention, and Applicants respectfully request that the rejection be withdrawn.

CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: _____
Deborah H. Yellin
Registration No. 45,904

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

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